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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/526,348	03/16/2000	Dr. Guido Bojack	514413-3817	2532

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EXAMINER

CRANE, LAWRENCE E

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 05/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/526,348	<b>Applicant(s)</b> BOJACK ET AL.	
	<b>Examiner</b> L. E. Crane	<b>Art Unit</b> 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on March 23, 2006 (amendment).
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1,8,13-17 and 22-34 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,8,13-17 and 22-34 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

Claim **4 and 18-21** and additional claims **2-3, 5-7 and 9-12** have been cancelled, claims **1, 8 and 15** have been amended, the disclosure has not been amended, and new claims **22-34** have been added as per the amendment filed March 23, 2005. No additional Information Disclosure Statements (IDSs) have been received as of the date of this Office action.

Claims **1, 8, 13-17 and 22-34** remain in the case.

The disclosure is objected to because of the following informalities:

Page one of the disclosure fails to indicate the foreign priority claim.

Appropriate correction is required.

Note to applicant: when a rejection refers to a claim **X** at line **y**, the line number “**y**” is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

Note #2 to applicant: In claims of more than one page in length, examiner suggests that line numbering which covers the entire length of the claim is useful for facilitating quick and accurate communication.

On May 3, 2006 examiner queried applicant by telephone concerning the structure being referred to by the term “(III-1)” at the end of claim **31**. Applicant replied that the noted term was incorrect and should have been --(V) --. The remainder of this Office action has been prepared assuming that this typographical error will be corrected in applicant’s next response.

Claims **1, 15, 22, 23, 26, 27, 28, 31 and 33** are objected to because of the following informalities:

In claim **1** at line 23, the newly inserted term “or” is superfluous and should be deleted. The identical term appearing at line 24 is sufficient. See also in claim **1** the same term at line 61 (superfluous) and the sufficient term at line 63.

In claim **1** at line 62, first substituent group, the included term “(O<sup>14</sup>)” appears to be incomplete. Did applicant intend the term to read -- (O-R<sup>14</sup>) -- or was an isotopic substituent being defined?

In claim 1 at line 37, the term “substituted” is grammatically incomplete and should be amended to read -- is substituted --. See also claim 22 at line 19; claim 23 at line 5; claim 26 at line 32; claim 27 at line 15; claim 28 at line 5; claim 31 at line 26; and claim 33 at line 26.

In claim 1 at line 65, the term ending with “phenyl” to be in properly alternative form should read -- or phenyl -- at its end.

In claim 1 at line 69, the presence of square brackets suggests the possibility that applicant intended deletion. Examiner suggests substitution of differently shaped brackets or a second set of parentheses to avoid possible problems should this application be allowed.

In claim 15 at line 1, the term “compoosition” is a misspelling of the term -- composition --.

In claim 22 at lines 8, 10, 18 and 26, there are extraneous marks (line through, underlining, duplicate punctuations) which appears to be unintentional additions to the claim. Removal of all unintended notations is respectfully requested.

Appropriate correction is required.

Claims 1, 8, 13-17 and 22-34 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of “undue experimentation” is appropriate are as follows.

A. The breadth of the claims is excessive in view of the number of specific embodiments listed in the Tables at pages 63-123 (11 examples) when compared with the total number of examples (a total of 698 separate examples are listed at pages 63-123).

B. The nature of the invention is compounds which are adenosine deaminase (ADA) inhibitors and/or adenosine monophosphate deaminase (AMPDA) inhibitors and their

administration to plants as a herbicide, but without any guidance concerning which disease conditions are to be treated and how such treatment should proceed, or what other plant growth is to be inhibited.

C. The state of the prior art varies widely, but in some cases is very limited because the synthesis of several of the bicyclic heterocycles is presently unknown in the prior art.

D. The level of one of ordinary skill also varies widely because of the wide variation in the amount of prior art available in either the synthetic or medicinal areas depending on the ring system selected.

E. The level of predictability in the art also varies widely because of the lack of information concerning how to make or use several of the heterocyclic systems included within the scope of the claims.

F. The amount of direction provided by the inventor is quite limited because the number of examples provided (only 11 compounds characterized), wherein only a subset were tested for biological activity, and none of these tests for biological activity were conducted on whole mammalian hosts (all *in vitro* tests) and no tests were conducted on any plants.

G. The existence of working examples is very limited with only 11 compounds prepared and characterized and only 5 tested for ADA activity using rabbit ADA.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure would be very substantial because of the lack of prior art teachings to guide the synthetic efforts where the bicyclic heterocycles are previously unknown and the almost complete absence of medicinal test data to guide experimentation concerning how best to effect ADA inhibition in a complete mammalian hosts. Examiner therefore concludes that, in the absence of considerably larger quantities of both synthetic and medicinal testing data, the instant claimed subject matter could only be practiced following expenditure of an undue amount of experimentation in both the synthetic and medicinal testing areas. In addition, the vast array of substituents, nested substituents, and inoperative embodiments like SF<sub>5</sub> (claim 1 at line 18, etc.; a very hydrolytically unstable substituent at best) make the task of the ordinary practitioner attempting to practice the instant invention even more difficult.

Applicant's arguments filed March 23, 2006 have been fully considered but they are not deemed to be persuasive.

Examiner notes with appreciation the extensive amendment and its appropriate effect on the scope of the instant claims. However, applicant has continued to insist on excessive large definitions of, for example variables "R, R<sup>o</sup>" which, among 38 alternative substituent groups 23 of which are subgeneric, includes at least one obviously inoperative and unenabled embodiment, "SF<sub>5</sub>." Examiner respectfully requests additional reduction of the very substantial numbers of alternative substituents, the vast majority of which are not enabled.

In addition, more specific claim language defining the variables "G," "L" and "X" is also needed as noted elsewhere in this Office action, and said language, if appropriately narrow in scope, would also contribute to overcoming this ground of rejection.

As noted in previous responses, examiner also finds the minimal descriptions of the particular chemical process steps to be entirely inadequate because there is insufficiently detailed instruction in the process claims directed to how the process steps are carried out, including failure to provide for a clear disclosure of the actual reagents required; e.g. "chlorinating agent" includes a substantial array of possible reagents many of which are inappropriate for the claimed process. And if examiner understands the process being conducted, POCl<sub>3</sub> is responsible for both dehydration and subsequent nucleophilic displacement by chloride ion, not merely "chlorination" as in the chlorination of ethylene; i.e. the term "chlorination" without more is misleadingly narrow in scope.

Claims **1, 8, 22-31 and 33** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Note to applicant: the amendment of claim 1 at lines 9-10 is much appreciated. Examiner suggests that a grammatically parallel clarifying amendment at lines 12-13 would make parts "a)" and "b)" of the definition of variable "E" equally clear.

In claim 1 at lines 54-58 (formerly lines 54-55) and lines 51-53, the interrelations between variables "G" and "L" are defined in a functional manner which hints at many possible chemical structures including those specified in the instant disclosure, but because

said definitions fail to define with particularity any structures whatsoever, the instant claim is lacking in adequately defined metes and bounds. See also claims **22-31 and 33**.

Applicant's arguments filed March 23, 2005 have been fully considered but they are not deemed to be persuasive.

In response to applicant's request for guidance, examiner suggests that this problem cannot be overcome with words alone but requires one or more structural representations. Examiner also recognizes that the disclosure may be defective in that there may be no descriptions covering the subject matter areas lying between the broad generalities now found in the definitions of "G" and "L" and the specific embodiments, in which case applicant may be limited to the specific embodiments.

In claim 1 at line 73, the term "substituted phenyl" is incompletely defined because the included term "substituted" implies subject matter which has not been provided for in the claim rendering the claim incomplete.

Applicant's arguments with respect to claim 1 have been considered but are deemed to be moot in view of the new grounds of rejection.

In claim 8 at lines 4 and 6, the term "reducing" is incomplete because the particular chemical process which appears to be implicated is a specific kind of reduction, namely removal of the "X" group by  
-- catalytic hydrogenolysis -- . Substitution of the suggested term is respectfully requested.

Applicant's arguments with respect to claim 8 have been considered but are deemed to be moot in view of the new grounds of rejection.

In claim 8 at line 8, the term "Z is a precursor of the radical G-L" is incomplete because this functional description fails to describe what the structure of "Z" is.

Applicant's arguments filed March 23, 2006 have been fully considered but they are not deemed to be persuasive.

Applicant is referred to the comments following the rejection of claim 1 because of deficiencies in the definitions of variable "G" and "L." The same problem seems to be present

here, namely that "Z" is only defined generically or specifically with a wide area wherein the disclosure fails to provide intermediate degrees of disclosure.

Claim 8 is incomplete because the term "modifying" at line 11 implies one or more chemical process steps but fails to completely describe the process step or steps implied.

Applicant's arguments filed March 23, 2006 have been fully considered but they are not deemed to be persuasive.

Applicant has responded with a request for suggestions. As above, examiner's view is that the disclosure has a large gap between the specific embodiments (specific examples supporting a narrow scope of coverage) and the generic disclosure (very broad and indefinite disclosure with lacks adequate support for its scope of coverage). Therefore, the only terminological suggestion to be made which would meet the requirements of 35 U.S.C. §112, first paragraph and second paragraph, would require applicant's agreement to the introduction of all of the particular steps (specific examples) implied by the generic term "modifying," and not trying to claim, and/or not expecting to get allowance of, the excessively broad and indefinite claim language now present in the case.

Examiner notes the introduction of the term "reacting" in place of the now cancelled "cyclizing," but finds these terms not sufficiently particular. Examiner suggests that the chemical process needs to be addressed. In the case of the ring formation described at the end of claim 8, the particular reactions is -- cyclization with the loss of water and ammonia --, and if there is any other reagent or catalyst present besides the amidine and the substituted azole reactants, this should also be specified at least generically (base, acid, etc.).

Claims 32 and 34 are rejected under 35 U.S.C. §112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Applicant appears to be claiming compounds made by the process defined in the parent independent claims, but has not styled the dependent claims as -- product by process -- claims. Examiner suggests that amendment to the product-by-process style will effectively address this rejection.



Applicant's arguments with respect to claims **1-3 and 5-17** have been considered but are deemed to be moot in view of the new grounds of rejection.

Claims **1, 8, 15-17 and 22-33** would be allowable if rewritten or amended to overcome the rejections under 35 U.S.C. §112.

Applicant and assignee of this application are required under 37 C.F.R. §1.105 to provide the following information that the examiner has determined is reasonably necessary to the examination of this application:

The information is required to document the level of skill and knowledge in the art of the reference or references which are the basis for the "except" exclusions of subject matter found at the end of new claims **26 and 27** in order for examiner to confirm that the proposed exclusions are appropriate, or to take other appropriate actions.

In response to this requirement, please provide the title, citation and copy of each publication that was relied upon to draft the claimed subject matter. For each publication, please provide a concise explanation of the reliance placed on that publication in distinguishing the claimed subject matter from the prior art.

In responding to those requirements that require copies of documents, where the document is a bound text or a single article over 50 page, the requirement may be met by providing copies of those pages that provide the particular subject matter indicated in the requirement, or where such subject matter is not indicated, the subject matter found in the applicant's disclosure.

The fee and certification requirements of 37 C.F.R. §1.97 are waived for those documents submitted in response to this requirement. This waiver extends only to those documents within the scope of the requirement under 37 C.F.R. §1.105 that are included in the applicant's first complete communication responding to this requirement. Any supplemental replies subsequent to the first communication responding to this requirement and any information disclosures beyond the scope of this requirement under 37 C.F.R. §1.105 are subject to the fee and certification requirements of 37 C.F.R. §1.97 where appropriate.

The applicant is reminded that the reply to this requirement must be made with candor and good faith under 37 C.F.R. §1.56. Where the applicant does not have or cannot readily obtain an item of required information, a statement that the item is unknown or cannot be readily obtained will be accepted as a complete reply to the requirement for that item.

The requirement is subject to the provisions of 37 C.F.R. §1.134, §1.135 and §1.136 and has a shortened statutory period of 3 months. EXTENSIONS OF THIS TIME PERIOD MAY BE GRANTED UNDER 37 C.F.R. §1.136(a).

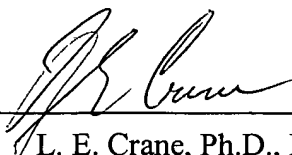
Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

LECrane:lec  
**05/05/2006**



L. E. Crane, Ph.D., Esq.

Patent Examiner

Technology Center 1600